

REMARKS/ARGUMENTS

Claims 1-16 and 33-36 are pending in this application. Claims 1, 13, 15-16 and 33 have been amended, and previously withdrawn claims 17-32 and 37-40 have been canceled. These amendments are made without prejudice to presentation of the original claims in a continuing application.

Claims 1, 15-16 and 33 have been amended to limit the activated phosphate moiety to a phosphoramidite. Support is provided in the specification on page 11, lines 3-6. No new matter is entered upon entry of these amendments.

I. Claim Rejections under 35 U.S.C. § 103

Claims 1-16 and 33-36 stand rejected under 35 U.S.C 103(a) as allegedly unpatentable over U.S. Patent No. 5,212,295 to Cook ("the Cook patent") in view of U.S. Patent No. 5,852,168 to Barany, *et al.* ("the Barany patent") and WO 99/64433 to Eleuteri, *et al.* ("the Eleuteri reference"). Applicant respectfully traverses this rejection because combining the teachings of the Cook and Barany patents, or the Cook patent and the Eleuteri reference, would not have produced any claimed invention. The Cook patent, for example, does not disclose, teach or suggest a method of the type claimed in which a 2'-substituted nucleoside having a **phosphoramidite** is used to prepare an internucleotide phosphorothioate linkage enriched in the Sp enantiomer by use of a coupling agent having a pKa ranging from about 3.3 to about 4.5. Rather, the Cook patent discloses methods involving **phosphate** chemistry for oligonucleotide synthesis. In addition, the Cook patent discloses the use of **basic** conditions to form internucleotide linkages, and thus is inconsistent with the teaching of the Barany reference. Scheme 1 in columns 13-16 of the Cook patent, for example,

discloses a phosphate containing synthon (compound 14) being treated with a base to produce an anionic synthon (compound 15), which is reacted with a phosphate-containing nucleotide (compound 2) to form the phosphate oligonucleotide (compound 16). The Barany patent, by contrast, discloses the acidic 5-ethylthio-1H-tetrazole activator (Barany patent at column 18, lines 11-16). Applicant respectfully asserts that one skilled in the art would not be motivated to substitute the base used in the phosphate-type process disclosed in the Cook patent with the acidic activator disclosed in the Barany patent to arrive at the claimed methods. Since the Cook patent clearly teaches away from the use of an acidic coupling agent, this rejection for alleged obviousness in view of the combination of the Cook and Barany patents is improper and should be withdrawn.

The rejection is also improper with respect to the Cook patent and Eleuteri reference because their combination, even if motivated, would not have produced any claimed invention. Indeed, the Office Action's proposed modification of the phosphate chemistry disclosed in the Cook patent with the protecting groups disclosed in the Eleuteri reference would not have produced a method of the type claimed in which a phosphoramidite is used. Since at least this claim element is not taught or suggested by the proposed combination of the Cook patent and the Eleuteri reference, this rejection for alleged obviousness is improper and should be withdrawn.

II. Conclusions

Applicant requests the Examiner to:

- (1) enter the amendments to claims 1, 13, 15-16 and 33, and cancel claims 17-32 and 37-40;

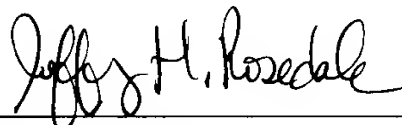
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- (2) reconsider and withdraw the standing rejections of the claims; and
- (3) pass claims 1-16 and 33-36 to allowance.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-5984.

Respectfully submitted,



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